

Most of the change we think we see in life is due to truths being in and out of favor.

Robert Frost  
The Black Cottage

OBESITY

# Pollutants May Put on the Pounds

The worldwide obesity epidemic is usually blamed on overeating and underexercising. But limited evidence has suggested a few environmental contaminants may also be playing a role. Now some of the first detailed evidence implicating organotins, a class of persistent compounds containing at least one tin-carbon bond, has been published in the September 2006 *Molecular Endocrinology*. A team of U.S. and Japanese researchers found both *in vitro* and *in vivo* evidence that exposure to a number of organotins, at concentrations typically found in people and wildlife, can contribute to alterations in pathways known to play a key role in excess weight gain, and can lead to significant aberrations in fat cells in mice and frogs.

As in many countries around the world, the percentage of people in the United States who are overweight and obese has been rising sharply in the past 30 years or so. Excess weight is strongly linked with many serious health problems, including heart disease, type 2 diabetes, high blood pressure, and some cancers. Prevention of obesity is by far the best available treatment. Preventing exposures to environmental contaminants over the course of a lifetime, even prior to conception, may be an important part of the battle, if this and other recent papers hold up to scrutiny.

Bruce Blumberg, an assistant professor of developmental and cell biology at the University of California, Irvine, and his colleagues studied organotins partly because of their endocrine-disrupting effects. Growing evidence suggests that some endocrine disruptors (such as bisphenol A and nonylphenol) can play a role in weight gain (although others, such as genistein, can protect against weight gain). Organotins are widespread through their use in boat hull antifouling paints, pesticides, wood preservatives, textiles (as a biocidal agent), plastics, and other products. Many studies have documented adverse health and environmental effects of organotins, from masculinization in some fish to hepatotoxicity in some mammals. Human exposure is largely through consumption of contaminated foods and contact with treated materials.

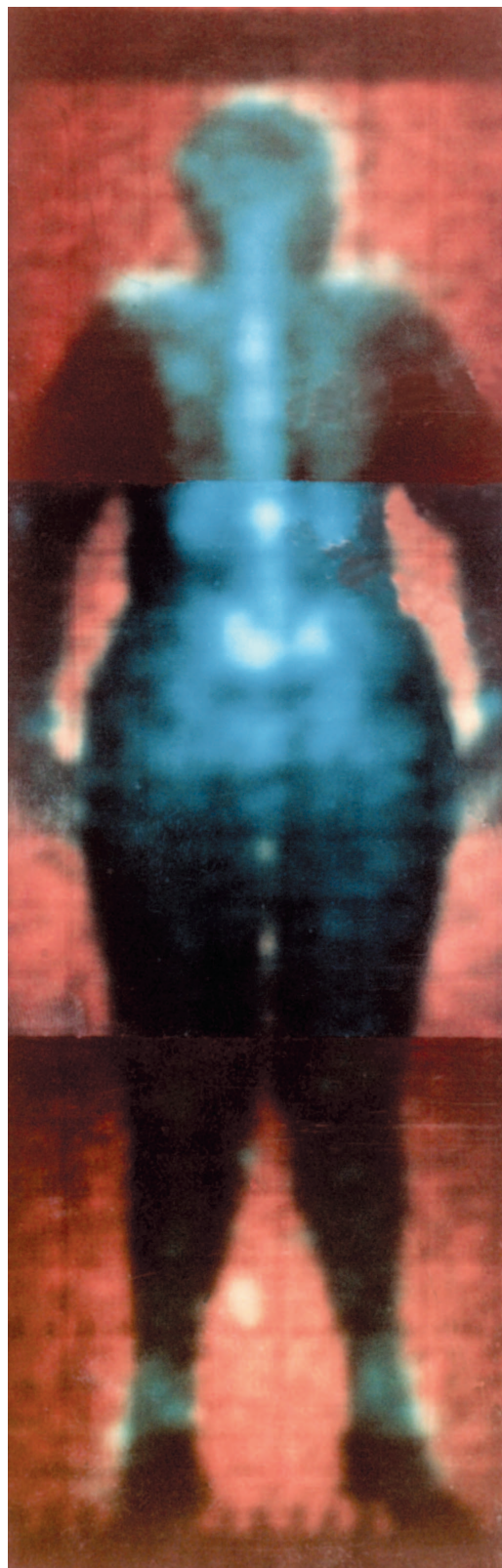
The team assessed several organotins to gauge their effects on weight gain, and found that a few, particularly tributyltin

chloride, were strongly implicated. Others, such as bis(triphenyltin) oxide, dibutyltin, tetrabutyltin, and the dialkyltins, also showed some effects. To varying degrees, *in vitro* and *in vivo* exposures in mice and frogs disrupted the normal function of retinoid X receptor  $\alpha$ ,  $\beta$ , and  $\gamma$  and/or peroxisome proliferator-activated receptor  $\gamma$ , all of which play key roles in a number of processes related to fat cell differentiation.

Exposure in neonatal mice also led to significant perturbation of signaling pathways and aberrant fat cell formation at several sites, including the liver, testis, and epididymis (where sperm are stored and become mature). *In utero* exposure in mice also led to greater accumulation of fat in several sites after the mice were born. Further, although the birth weight of mouse pups exposed *in utero* tended to be normal, at age 10 weeks the fat content in their epididymis was 20% higher than normal. Aberrant development of fat tissues around the gonads in both males and females also occurred in the frogs. These findings fit with research by others showing that humans can be underweight at birth, but can quickly become overweight, possibly because their fat cell content or function is aberrant.

The Blumberg team's findings are significant, and may be just the tip of the iceberg, says Paul Cooke, a professor of reproductive biology at the University of Illinois at Urbana-Champaign. Blumberg and colleagues observed that estimates of health effects based on structure-function relationships—typically used to gauge the effects of a group of chemicals—would not have predicted the observed effects of organotins since organotin structures do not resemble those of other compounds that activate retinoid X receptors and peroxisome proliferator-activated receptor  $\gamma$ . According to Cooke, the results therefore suggest that other chemicals that affect various hormone signaling pathways may play a similar role in weight gain.

—Bob Weinhold



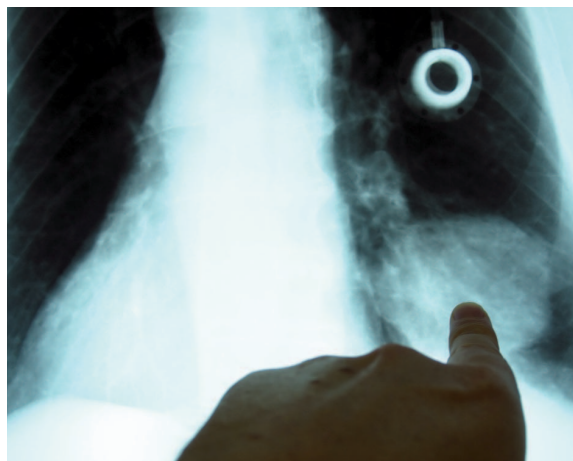
**Toxic tally.** New data suggest exposure to certain pollutants may exacerbate weight gain.

Getty Images

## ENVIRONMENTAL MEDICINE

## Blood Test to Detect Lung Cancer

Lung cancer kills more Americans each year than all leukemias and cancers of the breast, prostate, and ovary combined. But a new diagnostic that may allow early detection of the dominant form of the disease could change that grim picture. A team of researchers at the University of Kentucky Chandler Medical Center in Lexington led by Li Zhong, an assistant professor in the Division of Pulmonary, Critical Care, and Sleep Medicine, has developed a blood test



**Pinpointing lung cancer.** A new blood test may help doctors detect non-small cell lung cancers earlier.

for detecting non-small cell lung cancer (NSCLC), the disease associated with 80% of diagnosed lung cancers.

An estimated 175,000 new cases of lung cancer will be diagnosed in 2006, according to the American Cancer Society, and about 162,000 people will die of the disease. Fewer people are dying of NSCLC than in the past, which may reflect fewer people smoking. Still, those diagnosed tend to be diagnosed late, and those diagnosed late tend to die of the disease.

Spiral computed tomography (CT) imaging is today's gold standard for lung cancer detection, able to identify tumors less than 1 cm in diameter. But at more than \$400 a test, spiral CT imaging is far too costly for population-level screening. Further, there is growing concern that spiral CT imaging is overdetecting lung cancers that, left alone, would not progress, and might even regress. A better test would be one specific for cancers that are actively progressing.

Zhong's test, described in the July 2006 issue of the *Journal of Thoracic Oncology*, uses a panel of five cancer-associated protein markers identified by their reactivity to antibodies in cancer patients' blood. The markers were identified by generating a panel of proteins corresponding to genes expressed in NSCLC cells, then probing them with antibodies from NSCLC patients' blood. The five proteins that were the most discriminating—reacting to antibodies from patients much more than they reacted to antibodies found in the blood of nonpatients—were tested together for their ability to discern between blood samples drawn from diagnosed NSCLC patients and those from nonpatient controls.

Used together, the five markers form a "fingerprint" for cancerous samples, with a readout that is highly specific, able to separate cancer and noncancer samples in 87.5% of cases tested. By comparison, the widely hailed prostate-specific antigen test for diagnosing prostate cancer is just 36% accurate, and the CA125 test for ovarian cancer is 57% accurate. The new test can also recognize cancerous samples in earlier stages.

The cost of the new test will depend on the diagnostic platform ultimately developed, but is expected to be significantly less than the current standard. "We can lower the risk of people [progressing] to advanced-stage lung cancer," Zhong says. "If you can screen less expensively first, then you can suggest some people for follow-up—come back in six months and redo the test, or for some, go ahead and take the CT test now."

Jonathan Cohen, whose Rockville, Maryland, company 20/20 GeneSystems is developing the new test toward clinical application, is confident that the test could change outcomes. "A lot of diagnostic products stumble because they won't make a clear clinical impact," he says. "This is one where there's a significant unmet need and a clear and very compelling clinical utility."

Ruth Etzioni, a cancer statistician at the Fred Hutchinson Cancer Research Center in Seattle, recommends caution, though. Of this and the other new fingerprint diagnostics coming into use, she says, "The sensitivity and the ability to identify tumors is only the first step. Then whether it actually carries with it a significant benefit and a low harm profile is the key." —Victoria McGovern

## Debugging Without Methyl Bromide

Food and farming uses are among the few applications still allowed for the pesticide methyl bromide, which has been largely phased out under the Montréal Protocol. Now engineers at the University of California, Davis, have developed a new sterilization method for fresh produce that could replace post-harvest needs for this ozone-depleting chemical. The new method, metabolic stress disinfection, subjects pests to alternating vacuum and carbon dioxide treatments, which effectively suffocates the insects. Although the initial cost of the equipment is higher than methyl bromide, the chemicals used in the process are much cheaper. The gases used also can be recovered and recycled.



## EPA PM Standard Standoff

Internal documents from the EPA show that the agency could be protecting more lives each year if it had adopted stringent particulate air pollution standards advocated by an agency advisory panel. The documents reveal that 5,000–10,000 Americans could be saved from air pollution-related strokes, heart disease, and lung disease with stronger standards; instead, the agency opted in September 2006 to retain existing particulate rules. In a press release, the EPA said that the standards as set are still the most protective in history. The panelists disagree, however, and on 29 September 2006 sent EPA administrator Stephen Johnson a letter stating that "there is clear and convincing scientific evidence" that significant adverse human health effects occur at the current standards.

## The Biomonitor

On 29 September 2006 California governor Arnold Schwarzenegger enacted a statewide program, one that is both voluntary and confidential, to measure levels of chemical contaminants in people.

The program, the first of its kind in the United States, could be in place by 2007. Program data will make up a statewide report on environmental chemical exposures, and smaller studies on communities of concern and statewide trends will be conducted in future years as needed. Another program goal is to prioritize chemicals for study. A nine-member scientific panel appointed by Schwarzenegger and the state legislature will guide the program.





## LEAD

## Painting an Epidemic

The control of lead-based paint in residences has posed an ongoing public health challenge for decades. Now researchers have shown that several Asian countries are still selling paint with lead levels exceeding U.S. standards. The team warns in the September 2006 issue of *Environmental Research* that a worldwide ban on lead-based paint is needed to avoid perpetuating a global health epidemic. “By now, it is widely accepted around the world that lead should not be in paint,” says study head Scott Clark, a professor of environmental health at the University of Cincinnati College of Medicine.

Lead expert Bruce Lanphear, a professor of environmental health at Cincinnati Children’s Hospital Medical Center, says, “We know that many countries still do not have regulations for the lead content of either new paint or paint in existing housing. [Further,] it is both costly and difficult to reduce exposure from lead-based paint after it has been applied.” The United States has set limits of 600 ppm for lead in new paint for residential use and less than 5,000 ppm for paint in existing housing; paint containing at least 5,000 ppm lead is considered to be “lead-based.”

The effects of lead exposure depend on age (with children under 6 particularly vulnerable) and on whether the exposure is chronic or acute. In children, lead exposure can cause hyperactivity, anemia, brain

damage, and mental retardation, while adults may suffer increased blood pressure, hearing and vision impairment, and nerve damage.

Clark and colleagues analyzed 80 consumer paint samples of various colors and brands from stores in India, China, Malaysia, and Singapore to compare their lead content to U.S. standards. They applied a single layer of each paint to a wooden block, then transported the samples to the University of Cincinnati for analysis.

The percentages of paint samples exceeding the U.S. lead limit for new paint were 100%, 72%, 56%, and 9% for India, Malaysia, China, and Singapore, respectively. The first three countries have no regulatory limits in place, whereas Singapore limits lead in new paint to 600 ppm. Clark says some multinational paint companies offered leaded paints in the countries without lead regulations at the same time that they sold lower-lead paint in Singapore. Noting that many U.S.-based paint manufacturers sell their products in Asia and have partners in the region, he says, “American companies need to promote U.S. environmental standards abroad and encourage their partners to lower the lead content in paint and other consumer products.”

Stephen R. Sides, vice president for environmental health and international affairs with the Washington, DC-based National Paint and Coatings Association, says, “We are sharing the findings of Dr. Clark’s study with the U.S. paint industry to make it aware of the lead paint-related concerns and public health issues in Asia. Hopefully, U.S. paint companies will ensure that their products aren’t contributing to the problems.” —Ron Chepesiuk

## FOOD SAFETY

## Pop Toxicology?

Excessive consumption of carbonated soft drinks has been putatively linked to health effects including dental caries, obesity, and osteoporosis. An August 2006 study by the Centre for Science and Environment (CSE), a private research group in New Delhi, now reiterates another concern first raised three years ago: pesticide contamination.

In *Analysis of Pesticide Residues in Soft Drinks*, the authors report finding an average pesticide content of 11.85 ppb in 11 soft drink brands sold in India by The Coca-Cola Company and PepsiCo. An average of 5.37 ppb lindane, a possible human carcinogen, was detected in the 57 samples analyzed, as was an average of 4.71 ppb chlorpyrifos, a neurotoxicant. Heptachlor was found in 71% of the samples at an average concentration of 0.41 ppb. All these values surpass safe limits of 0.1 ppb for individual pesticides and 0.5 ppb for total pesticides in soft drinks that were proposed by the Bureau of Indian Standards in October 2005. The CSE had released similar findings in 2003.

Industry has contested the findings. Coca-Cola commissioned the analysis of more than 180 samples at Central Science Laboratory (CSL)—a British executive agency—and Vimta Labs in India, and the

results showed less than 0.1 ppb of any pesticide. John Gilbert, research director for food at the CSL, says the CSE did not achieve sufficiently good matches between compounds in the samples and known pesticides to confirm identification. “If an identification is not confirmed unequivocally,” he says, “then going on and measuring something of uncertain identity makes no scientific sense.”

In October a panel of India’s health ministry examined the report and rejected the

solids and liquids without validating it for soft drinks. The panel said data received from the CSE relating to “percentage of recovery of different analytes” differed from those in the August 2006 report, raising doubts about the reliability of the results.

Sapna Johnson, lead author of the CSE report, defends the findings, saying they were quantified by two separate detectors. She thinks one reason for the difference in findings of the two studies may be that the CSE used GC-MS only for confirmation of pesticides, whereas the CSL used GC-MS for quantification as well. A CSE statement on the methodology reads, “Test products are fortified with target compounds and are analyzed to demonstrate precision and accuracy of the analyses. Replicate analyses of samples are conducted to confirm that the original results are reproducible. This is how the world tests products. And this is a scientifically valid and socially prudent method.”

“Although the levels of pesticide residues reported [in the CSE] study are unlikely to cause immediate harm to consumers, chronic effects following long-term exposure may occur, particularly in susceptible populations such as children,” says Rolf U. Halden, cofounder of the Johns Hopkins Center for Water and Health. He says the CSE’s data may hint at a larger problem—pesticide-impacted drinking water in the region—and that confirmatory analyses using the best available analytical techniques should be the next step. —Dinesh C. Sharma



**Thirst-quencher threat?** People enjoying soft drinks outside the Golden Temple in Amritsar, India. A controversial new report finds that soft drinks made in India may contain high level of pesticides.

findings, noting that confirmation of pesticide residues in soft drinks by gas chromatography-mass spectrometry (GC-MS) analysis was done for only three samples and did not represent the pesticide residue status of all the 57 test samples. In addition, the CSE improperly used U.S. EPA methodology meant to estimate pesticide concentrations in

ehpnet

## Massachusetts Toxics Use Reduction Institute

The Massachusetts Toxics Use Reduction Institute (TURI), based at the University of Massachusetts Lowell, is the research and education arm of a three-part program established by the state's 1989 Toxics Use Reduction Act (the program also includes regulatory and onsite consultation components). The TURI website at <http://www.turi.org/> describes the institute's work in reducing the amount of chemicals used in manufacturing processes in Massachusetts, information that may be useful for those outside the state as well. By companies' estimations, TURI helped reduce the amount of chemicals used by 41% since 1990 while at the same time helping companies improve their competitiveness. The institute reports that by-products from cleaning processes have been reduced during the same time period by 65%, and onsite chemical releases have dropped by 91%.

One of the newest TURI projects is the CleanerSolutions online database of surface cleaners, developed by the TURI Laboratory to help users identify safer cleaning products that perform as well as conventional products. A link to the CleanerSolutions website (<http://www.cleanersolutions.org/>) is found in the

Online Tools section of the TURI homepage. The database contains 10 years' worth of product testing information that is combined with health and environment indicators. The CleanerSolutions page on the TURI website also includes short interactive tutorials for using the database, a directory of other alternative cleaning online tools, and a section for vendors to propose items for inclusion in the database. Visitors can search the database for cleaning alternatives by either the contaminant to be removed, the solvent to be replaced, the type of equipment to be used, or the material to be

cleaned. The TURI Laboratory conducts preliminary screening to determine potential risks of alternative chemicals based on global warming potential, ozone depletion potential, volatile organic content, flammability and reactivity, and acute toxicity.

The TURI website also has a Browse Topics page that catalogs information on the many projects the institute is working on. The categories listed include bio-based materials, cleaner production, competitiveness, corporate reporting, environmental management systems, nanotechnology, sustainability, and worker health and safety. The Corporate Reporting section includes an investor's perspective on the value of sustainability reporting in socially responsible investing as well as case studies on how two companies have employed sustainability reporting or toxics use reduction in their activities.

Visitors can also find information on the TURI website using the links on the left side of the homepage to go to sections on Industry, Community, Government, TURI Training, the TURI Laboratory, Toxics Use Reductions Act Data, and the TURI Library. Available within the Research portion of the Industry section is the recently completed Five Chemicals Alternatives Assessment Study. This study was requested by the Commonwealth of Massachusetts to assess safer alternatives for lead, formaldehyde, perchloroethylene, hexavalent chromium, and di(2-ethylhexyl) phthalate. Along with the report is a Frequently Asked Questions page and documents related to the project. The Community section includes numerous fact sheets and other resources offering information on safer alternatives in areas such as auto maintenance and repair, construction, restaurant kitchen management, and household cleaning. This section also includes several sample policies, including one for schools and another for municipal pest management. —Erin E. Dooley



TOXICS USE  
REDUCTION  
INSTITUTE

## Musician Spreads Word About Water

UN statistics show that nearly 2 million children die each year because of unclean water supplies and poor sanitation. Now popular musician Jay-Z is set to star in a documentary titled *Diary of Jay-Z: Water for Life*, part of a larger educational program on global issues sponsored by the music channel MTV. The documentary will be shot during Jay-Z's world tour, when he will be visiting areas in Turkey, South Africa, and other countries without access to safe drinking water. The program will also feature projects that are working on sustainable solutions to the problem, and will call on viewers to take action by helping abroad and at home. MTV and the UN will augment the program with a special website, free classroom access to the documentary, and supporting lesson plans.



## Inventorying Emissions in Mexico

September 2006 witnessed the publication of Mexico's first national inventory of atmospheric air emissions, which was produced with support from the Commission for Environmental Cooperation and U.S. partners. The inventory provides detailed data on nitrogen oxides, sulfur dioxide, volatile organic compounds, carbon monoxide, ammonia, and particulate matter for each Mexican state and municipality. The report covers industrial, mobile, and natural sources of these pollutants. The inventory, part of a five-year effort to standardize air emissions reporting across North America, is a key step toward improving air quality management both within Mexico and on each side of its borders.

## New Hope for Nepal's Environment

Over the past decade, ongoing civil war between Maoist and government forces in Nepal has disrupted many conservation activities in the country. A ceasefire was declared in May 2006, however, and a month later the parties agreed to establish a new interim government and draft constitution. At this point, advocacy groups including WWF Nepal, CARE Nepal, and the IUCN drew up a set of recommendations for preserving biodiversity, forest areas, and reserve lands in the country, which the constitutional committee agreed to incorporate into the draft constitution. Among other recommendations are a call to keep up to 40% of Nepal's land under forest cover in perpetuity, and to provide for investments in conservation and sustainable use of areas of biodiversity.

